REMARKS

Claims 18-23 are pending in this application. Claims 18-23 were rejected. The Examiner made the following rejections:

1) The Examiner sustains the rejection of claims 18-23 in view of nonstatutory type double patenting.
2) The Examiner rejects claims 18-23, under 35 U.S.C. § 102(b), as anticipated in view of U.S. Patent No. 6,043,244 to Caruso or U.S. Patent No. 5,855,907 to Peyman.
3) The Examiner rejects claims 18-23, under 35 U.S.C. § 103(a), as allegedly unpatentable in view of U.S. Patent No. 6,043,244 to Caruso as combined with U.S. Patent No. 5,855,907 to Peyman.

The Applicants' remarks are presented in the same order as the rejections set out above.

1) Applicants File a Terminal Disclaimer

The Examiner has rejected claims 18-23 for alleged obviousness type double patenting in view of U.S. Patent No. 6,685,951. In order to advance their business interests and without acquiescing to the Examiner's arguments, Applicants file herewith a Terminal Disclaimer Under 37 C.F.R. §1.321(c). Through this Terminal Disclaimer, the Applicants disclaim the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§ 154 to 156 and 173 of U.S. Patent No. 6,685,951. Applicants note this disclaimer traverses all of the rejections, raised under the judicially created doctrine of obviousness-type double patenting, as set out above.

2) The Examiner Admits the Claims Are Not Anticipated

The Examiner is reminded that, "for a reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a *single* reference." *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990) (emphasis added). It is axiomatic, therefore, that a reference cannot anticipate if this single reference fails to disclose an element of the claimed embodiments of the present invention.

Undeterred by this well settled standard for anticipation, as set out above, the Examiner states:

> "the primary reference, Caruso, teaches the general method described above. The secondary reference Peyman, teaches a method of treatment of migraine comprising anti-inflammatory compounds include (sic.) steroids, particularly glutocorticoids, for example, cortisol, cortisone, prednisolone, dexamethasone etc."

and,

> "it is the position of the examiner that the combination of the prior art reference is proper and the reference recited teaches the limitations of the instant claims."[1]

It is nonsense to speak of the "combination" of a "primary" with a "secondary" reference in the context of a rejection under 35 U.S.C. § 102(b). That is to say, if the Examiner is using the disclosure of a "steroid" in Peyman (i.e. the alleged "secondary" reference) to fill the gap[2] created by the absence of the same in Caruso[3] then Caruso, as a matter of law, cannot anticipate the invention as claimed. Similarly since Peyman fails to disclose a co-formulation[4] of dihydroergotamine with a steroid, Peyman must also fail as a reference which anticipates the claimed embodiments of the present invention.

3) The Claims Are Not Obvious

A) The Incorporation of Steroids is Not Taught by the Art Previously Cited by the Examiner.

In the Office Action mailed April 28, 2005, the Examiner recycles (almost verbatim) the rejections previously raised, in the Office Action mailed June 17, 2004, in view of the obviousness rejection raised as supported by U.S. patent 6,043,244 to Caruso. The Applicants note that each of the pending claims recite the administration of a formulation[5] comprising, in part, dihydroergotamine and a steroid. However, the teachings in U.S. patents 6,043,244 to

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1 Office Action mailed April 28, 2005, p. 4.

2 With regard to the disclosure of the elements in the claimed embodiment of the present invention.

3 Further, as the Applicants note in their rebuttal of the pending rejections raised under 35 U.S.C. 103(a), Caruso not only fails to disclose the use of steroids but actually teaches away from the same.

4 Similarly, Peyman not only fails to disclose a co-formulation of co-formulation of dihydroergotamine with a steroid but also teaches about the hazards of dihydroergotamine administration as a prelude to describing opioid co-formulations.

5 In a method for treating migraines.

Caruso are completely silent regarding the co-formulation of a steroid with any of the anti-migraine therapeutics taught therein or in methods for administering the same.

While the Examiner discusses Caruso with respect to the alleged disclosure of a fast dissolving formulation comprising dihydroergotamine, the Examiner points to nothing in this reference that would render obvious the administration of a co-formulation of dihydroergotamine *and a steroid* in methods for the treatment of migraine. The Examiner is completely silent on how Caruso teaches, or even suggests, the co-formulation of a steroid into any of the compositions taught therein. Indeed, the Applicants note Caruso teaches:

> ". . . in addition to the antimigraine drug and antimigraine- potentiating amount of an NMDA receptor blocker or substance that blocks a major intracellular consequence of NMDA receptor activation, the therapeutic composition herein can contain at least one other pharmacologically active substance e.g., caffeine (a stimulant), an antiemetic drug such as metoclopramide, domperidone, belladonna alkaloids and phenothiazines such as chlorpromazine, prochlorperazine, and promethazine, a non-narcotic analgesic, e.g., acetaminophen or a nonsteroidal anti-inflammatory drug such as aspirin, diclofenac, diflusinal, etodolac, fenbufen, fenoprofen, flufenisal, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamic acid, mefenamic acid, nabumetone, naproxen, oxaprozin, phenylbutazone, piroxicam, sulindac, tolmetin, zomepirac, and the like."

This laundry list of "additional active ingredients", however, fails to disclose steroids. The Examiner is reminded that in determining the propriety of the Patent Office case for obviousness, it is necessary to determine whether or not the referenced teachings would appear to be sufficient for one of ordinary skill in the relevant art to make the proposed substitution, combination or other modification in question. Surely it is not the Examiner's position that a list which fails to disclose a claim element, as either a genus or a species, is sufficient to render the same as obvious.

In contrast, as previously noted,[6] the Applicants appreciate that steroids have beneficial therapeutic properties[7] (vis-à-vis the treatment of migraine) and that sublingual administration of steroids allows for a prospective reduction of dose (and, thereby, reduction of side effects and toxicities) given: i) the direct transmucoal delivery into the bloodstream and ii) a reduction of the

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6 See, Applicants Response filed on December 16, 2004.

7 The Applicant also notes there is no obligation to describe the underlying mechanism of he claimed methods and the following remarks in no way limit the scope of the invention as claimed.

first pass effect associated with enteral administration. For example glucocorticoids, in part, stimulates gluconeogenesis and inhibits the uptake of glucose from muscle and adipose tissue. These physiological effects would be desirable in supplementing the action of DHE in methods for the treatment of migraine.

The '244 patent to Caruso would likely lead an investigator in a direction divergent from the path taken by the Applicants. Given the list of anti-inflammatory compounds Caruso *does* disclose, it is reasonable to infer Caruso's silence regarding steroids (many of which are potent anti-inflammatory agents)[8] is because the incorporation of steroids is inapposite to the compositions and methods taught by Caruso in the '244 patent. Moreover, one of ordinary skill in the art, confronted with Caruso's teaching regarding anti-inflammatory compounds, would note that all of these compounds[9] are within the genus of *nonsteriodal* anti-inflammatory.

Therefore, one of skill in the art would likely be discouraged from attempting the substitution suggested by the Applicants (e.g. the co-formulation of dihydroergotamine with a steroid) given steroid co-formulations are outside the only genus Caruso teaches as suitable anti-inflammatory compounds. This reference provides evidence of the *non-obviousness* of the claimed embodiments of the present invention and, therefore, rebut the very rejections[10] for which there were cited. See, *In re Gurley,* 27 F.3d 551, 553, 31 U.S.P.Q.2D (BNA) 1130, 1131 (Fed. Cir. 1994).

B. The Teachings in U.S. Patent 5,855,907 to Peyman are of no Moment

Peyman teaches the co-formulation of "an effective amount of an opioid" with five different categories of drugs: i) vasoconstrictors, ii) antiinflamatories (including steroids), iii) antimicrobials, iv) non-opiate antimigraine drugs, and v) decongestants.[11] As the Examiner notes, Peyman teaches "a method treatment of migraine comprising the topical administration of *an opioid* with combination of anti-inflamatory compounds include (sic.) steroids, particularly glucocorticoids, for example, cortisol, cortisone, prednisolone, dexamethasone and the like."[12] (emphasis added). However, Peyman is completely silent on the formula of *dihydroergotamine*

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8 Including, but not limited to, cortical and cortisone as currently claimed (in part) in pending claim 22.

9 aspirin, diclofenac, diflusinal, etodolac, fenbufen, fenoprofen, flufenisal, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamic acid, mefenamic acid, nabumetone, naproxen, oxaprozin, phenylbutazone, piroxicam, sulindac, tolmetin, and zomepirac.

10 Raised under 35 U.S.C. 103(a).

11 See, U.S. patent 5,855,907, Cols. 5 and 6.

with a steroid. Moreover, in the background section, Peyman teaches that:

> "[t]here are also specific antimigraine treatments, which include ergotamine and its related compounds, such as sumatriptan and dihydroergotamine, which are agonists of 5-HT(1B) and 5-HT(1D) receptors. Sumatriptan is administered orally, by subcutaneous injection, or as a nasal spray. Dihydroergotamine is administered intramuscularly, or as a nasal spray. These treatments are associated with the risk of coronary vasospasm."

Peyman identifies an undesirable side effect (i.e. coronary vasospasm) experienced by some patients with certain types dihydroergotamine administration and uses this teaching as a departure point to discuss the use of *non-dihydroergotamine* containing opioid co-formulations in the treatment of migraine. Peyman's: i) advisory regarding the (undesirable) side effect of dihydroergotamine administration and ii) silence on formulating dihydroergotamine with a steroid teaches away for the claimed embodiments of the present invention. That is to say, the '907 patent would likely be discourage one of skill in the art from attempting the co-formulation suggested by the Applicants. Therefore, the '907 patent to Peyman may not sustain a rejection under 35 U.S.C. 103(a).

C. The Examiner Still Fails to Make a Prima Facie Case for the Obviousness for the Claimed Embodiments of the Present Invention.

The Examiner states that, "[t]he Examiner is using knowledge of the two references cited herein"[13] to support the pending rejections under 35 U.S.C. 103(a). However, as the Applicants note above, this very same art is either silent on or teaches away from the use of at least one element recited within the pending method claims. If the cited art fails to provide the knowledge required to recapitulate the invention as claimed, the Applicants respectfully submit the

12 Office Action mailed April 28, 2005, p. 6.

13 *Id.*

Examiner is using the knowledge only provided by the Applicants' specification to render obvious the claims in the same. This is error. The Examiner is reminded that,

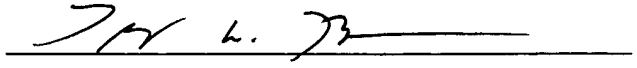
> "[t]o imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303, 312–13 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)

Moreover, "the mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." *In re Fritch*, 972 F.2d 1260, 1266, 23 USPQ 2d 1780, 1783–84 (Fed. Cir. 1992). Given the particularity with which the Applicants have documented: i) the elements of the claimed embodiments of the present invention not found in the cited art, ii) the failure of this same art to suggests a combination or modification which would recapitulate the invention as claimed, and iii) selected instances where this same art teaches away from the claimed embodiments of the present invention; the Applicants respectfully request the pending rejections be withdrawn and the claims passed to allowance.

CONCLUSION

Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect.

Dated: August 29, 2005



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